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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,676	04/08/2002	Sam Fong Yau Li	2577-118	7819

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EXAMINER	
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ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 03/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,676	LI ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *43-72* is/are pending in the application.

4a) Of the above claim(s) *62 and 66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-61, 63-65 and 67-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *04/02, 12/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, and subgroups I-A and I-i in the paper filed on November 24, 2003 is acknowledged. The traversal is on the ground(s) that the art does not teach the application of piezoelectric detector for the detection of an infectious agent associated with a veterinary disease, as indicated in the amended claims, or for the detection of S. enteritidis in particular. This is not found persuasive because the art does teach the use of such devices in immunoassays in general, and in particular, suggests the use of such devices for the detection of infectious diseases. See e.g., Larue et al., U.S. Patent 5,705,399, abstract, and column 11 lines 11-27. Thus, the common technical feature, the detection of an infectious disease using a piezoelectric detection device, is taught by the art.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 62 and 66 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

3. Currently, claims 43-61, 63-65, 67-72 are pending to the extent that they read on the elected inventions.

Information Disclosure Statement

4. The information disclosure statements (IDS) submitted on April 8, 2002 and on December 9, 2003 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner.

5. It is noted that only pages 1067-1071 of the Ye reference in the April 2002 IDS were submitted. Thus, the reference has been considered only to the extent of the submitted pages, and not the complete article.

6. The following reference is in a foreign language accompanied by an English abstract. Due to this, the reference has been examined only to the extent of the disclosure in the abstract.

DE 4436910, reference AN on the December 2003 IDS.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 43-61, 63-65, and 67-72 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection is primarily concerned with the language of claim 51, which describes the method of claim 43 wherein the immobilization comprises the adsorption onto a metal modified crystal. It is unclear what is meant by a metal modified crystal.

This is for two reasons. First, it is unclear if the term "metal modified" includes or is in addition to the attachment of the electrodes to the Pz crystal. If the former is correct, then the claims would appear to read on methods of performing the immunodiagnostic test wherein the Pz crystal has not been attached to electrodes, disclosed in the art and the application as required to induce the resonance used for the measurements needed to perform the claimed assay. App., page 10. However, because claim 51 implies through the doctrine of claim differentiation that the

Pz crystal need not be metal modified, it is not apparent how the method would operate if the Pz is not metal modified.

Second, if the metal modification allowing adsorption of the antigen/antibody is other than the metal electrodes, it is not clear what the scope of such modification entails. This is because, while the Applicant has disclosed the adsorption of the antigen/antibody to the bare metal electrodes (pages 11 and 17), there does not appear to be any discussion of metal modifications other than the attachment of the electrodes to the crystal and the attachment of the antigen/antibody to the electrodes in the specification. Thus, the Applicant has not provided sufficient description of what constitutes a metal modification such that the embodiments comprising such a modification have been particularly pointed out and distinctly claimed. Those in the art have not been made aware of the metes and bounds of the claimed invention.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 43-61, 63-65, and 67-72 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is based on the claim language of claims 43 and 51 as described above. In particular, the rejection is concerned with the language indicating that the Pz crystals need not be metal

modified (i.e. the metal modification includes the attachment of the electrodes, and is optional as indicated in claim 51). As indicated above, the art (see e.g. Bastiaans et al., U.S. Patent 4,735,906, of record in the April 2002 IDS; and Larue, U.S. Patent 5,705,399) and the specification (pages 2-5) teach that the metal electrodes attached to the crystal are necessary for the claimed method to operate. This is because these electrodes provide the energy required to induce the resonance of the crystal, which in turn is required to make the readings necessary for the claimed immunodiagnostic test operable. Thus, the Applicant is not enabled for the claimed methods or kits wherein the Pz crystals are not metal modified.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 43, 45, 47-50, 52, 53, 59, 60, 63, 67-69, and 71 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Bastiaans et al., (U.S. Patent 4,735,906, of record in the April 2002 IDS), in view of Larue (U.S. Patent 5,705,399) and Thorns (U.S. Patent 5,510,241). The claims read on methods for performing immunodiagnostic tests against S. enteritidis comprising attaching a antigen, or antibody against an antigen, of the bacterium to a piezoelectric (Pz) crystal, exposing the crystal to a sample, and determining if the pathogen is

present based on changes to the resonant frequency of the crystal before and after such contact. The claims also describe kits comprising the Pz crystal device used in the claimed methods.

Bastiaans teaches the use of PZ crystals in immunodiagnostic tests. See e.g., columns 1-3. The reference teaches methods that are substantially similar to those used in the present application in that one compound of a binding pair (e.g. an antibody or antigen) is bound to the crystal, which is then exposed to a sample to detect the presence of the binding partner. See, claims 1-18. The reference further teaches that used crystals may be cleaned and reused, and that the Pz crystal resonance measurements may be made using a universal counter. Column 4, lines 7-11, and 43-46. Similar teachings are also provided in Larue (abstract, columns 1-5), which also suggests the use of the Pz devices for the detection of antigens of illnesses, including those caused by Salmonella infections. Column 11, lines 11-27. Larue also specifies both that a preferred crystal is an AT cut quartz crystal and that the electrodes of the device are preferably gold, but may also be silver or another of a select group of metals. Column 2 lines 61-63, and columns 8-9. Each of these references also teaches that, after use, the devices may be cleared of bound antibody/antigen using compounds with high ionic strength (including sodium chloride solutions), or low ph. Bastiaans, col. 6 lines 17-30; Larue, col. 16 lines 43-48. It would therefore have been obvious to those in the art to use the compounds indicated by the application to perform such regeneration of the device. Thus, Bastiaans and Larue reference teach the method steps and the device described by the indicated claims, although they do not specifically suggest the use of such methods or devices for the detection of S enteritidis infection.

Thorns teaches methods of detecting S. enteritidis based on the detection of antibody/antigen binding and teaches the use of a test kit comprising antibodies against such

antigens "immobilized on a solid carrier." While the reference does not teach the use of Pz crystal devices, the reference indicates that the antibody/antigen binding diagnostic test may be carried out through any means known to those in the art. Column 7, lines 34-41. Because Larue indicates that the Pz devices may be used for the detection of Salmonella infections, and because both Larue and Bastiaans teach methods and devices concerned with the detection of analytes through antibody/antigen binding, it would have been obvious to use the methods and devices of these references for the detection of S. enteritidis using the antibodies disclosed by Thorns.

13. Claims 43-45, 47-50, 52, 53, 59, 60, 63, 64, and 67-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Bastiaans et al., (U.S. Patent 4,735,906, of record in the April 2002 IDS), in view of Larue (U.S. Patent 5,705,399) and Rajashekara et al. (WO 98/03656). The claims have been described in part. In this rejection, it is noted that certain dependant claims require that the S. enteritidis antigen adsorbed to the crystal is a recombinant antigen. The teachings of Bastiaans and Larue have also been described above. As indicated above, while these references suggest the use of the Pz crystal devices and methods for the detection of Salmonella infections, they do not specifically indicate the use of these inventions for the detection of S. enteritidis.

Rajashekara teaches the making and use of a recombinant antigens of Salmonella enteritidis and antibodies thereto. Pages 12-13, and claims 6 and 9. The reference also teaches the use of such antigens for the detection of S. Enteritidis infection through the detection of antibodies in an animal using the recombinant antigen. Claim 1. It is noted that the reference does not teach the attachment of the antigens to Pz crystals. However, in view of the teachings of

Larue and Bastiaans indicating the use of Pz crystal devices for the detection of Salmonella infections, and the use and attachment to the Pz crystals of antigens such that analytes, including Salmonella, may be detected, it would have been obvious to those in the art to use the antigens disclosed by Rajashekara in the methods and devices of Larue and Bastiaans.

14. Claims 46, and 54-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bastiaans in view of Larue and further in view of either Thorns or Rajashekara as applied to claims 43, 45, 47-50, 52, 53, 59, 60, 63, 67-69, and 71 or claims 43-45, 47-50, 52, 53, 59, 60, 63, 64, and 67-72 above, and further in view of Willner et al. (WO 98/40739, Willner I- of record in the April 2002 IDS). Claims 46 and 54-58 describe the method of claim 43 wherein the method comprises additional steps of adding a blocking reagent to the crystal. The teachings of the previously indicated references do not appear to teach the use of such blocking agents. However, Willner I, which also teaches the use of piezoelectric crystal devices to perform immunoassays, does suggest the use of such blocking agents. At page 7of the reference, Willner I teaches that such blocking reagents may be necessary to prevent non-specific binding to the crystal surface which may affect the performance of the assay. Thus, this reference, in combination with the other references indicated above, renders obvious the claimed inventions.

15. Claim 51 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bastiaans in view of Larue and further in view of either Thorns or Rajashekara as applied to claims 43, 45, 47-50, 52, 53, 59, 60, 63,67-69, and 71 or claims 43-45, 47-50, 52, 53, 59, 60, 63, 64, and 67-72 above, and further in view of Willner et al. (WO 97/04314, Willner II- of record in the April 2002 IDS).

Claim 51 requires that the antigen or antibody of claim 43 be immobilized on the Pz crystal by way of adsorption to a metal modified crystal. For the purpose of this rejection, the claim language "metal... modified crystal" is interpreted as requiring a metal addition to the Pz crystal other than the electrodes. The teachings of Bastiaans, Larue, Thorns, and Rajashekara have been described above. These reference do not teach the modification of the Pz crystal with a metal other than the addition of the electrodes to the crystal.

Willner II, however, teaches a Pz crystal device for use in immunoassays wherein the antigen or antibody is bound to a metal plate that "may be the same or different than" the electrodes. Abstract. Thus, the reference teaches the immobilization of the antigen/antibody by means of physical adsorption onto a metal modified crystal. Because the device and methods described by this reference are described as an alternative embodiment to the methods and devices of the Pz devices described by Bastiaans and Larue, it would have been obvious to those in the art to use the device of Willner in the methods and kits for the detection of S. enteritidis suggested by the teachings of the other indicated references.

16. Claims 61 and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bastiaans in view of Larue and further in view of either Thorns or Rajashekara as applied to claims 43, 45, 47-50, 52, 53, 59, 60, 63,67-69, and 71 or claims 43-45, 47-50, 52, 53, 59, 60, 63, 64, and 67-72 above, and further in view of Masten et al., J Bacteriol 175: 5359-65 and in view of Protein Accession CAA78777. Claims 61 and 65 further limit the method of claim 43 (and the kit for use in the method) to embodiments wherein the antigen comprises SEQ ID NO: 2. None of the previously identified references teach a protein with this sequence.

Protein accession number CAA78777 discloses a S. enteritidis flagellin comprising this sequence. SEQ ID NO: 2 falls within the central region of the protein disclosed (residues 252-342 of 504 residues). The Masten reference teaches the homology among the flagellin proteins of several Salmonella bacterium. In particular, the reference teaches that these proteins are highly antigenic (abstract) and that the regions with the most variability among the difference bacteria are found between residues 181 and 420 (pages 5363, and 5364). In view of the teaching that these proteins are highly antigenic, it would have been obvious to those in the art to use these proteins as targets for immunodiagnostic assays.

Because Rajashekara teaches that S. enteritidis is disclosed as the dominant Salmonella serotype in food poisoning, and that the best way to prevent human infection is to diagnose and treat animals prior to human consumption, the reference provides motivation for the application of the methods of Bastiaans and Larue for the detection of this bacterium. Masten teaches that the central regions of the protein show the most heterogeneity. It would therefore also have been obvious to use polypeptides including these regions of the proteins as either targets of ligands in such assays. Because SEQ ID NO: 2 is disclosed as an S. enteritidis sequence falling within such a region in Accession CAA78777, it would have been obvious to those in the art to use antigens comprising this sequence in methods for the detection of S enteritidis as suggested by the other references. Claims 61 and 65 are therefore obvious over the indicated references.

Conclusion

17. No claims are allowed.

18. The following prior art reference is made of record and considered pertinent to applicant's disclosure. However, while relevant the reference is not used as a basis for rejection for the stated reasons.

> Andle et al., U.S. Patent 6,033,852. This reference teaches a piezoelectric assay device that has been modified by the addition of a metal layer onto which the antigen/antibodies are deposited. The reference is considered to be similar in teachings to the Willner II reference.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

James C. Housel
3/22/04